AN EASY AND ABSOLUTE DIAGNOSIS FOR THE COUMARIN/CHROMONE DISCRIMINATION BY USING OXYGEN-17 NMR

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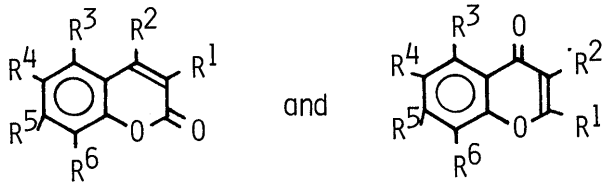
^{17}O-NMR at natural abundance was, for the first time, employed so effectively for the characterization between coumarins(I) and chromones(2).

KEYWORDS ^{17}O-NMR; coumarin/chromone discrimination; natural abundance; double-check technique; chemical shift difference

In spite of many reported procedures[1] for both benzo-α-pyrones(1) and benzo-γ-pyrones(2), new and reliable methods[2] are still being strenuously exploited because some known procedures have caused too much confusion in determination of the products, that is, the expected coumarins or chromones were not always obtained exclusively. Accordingly, when either the method or the compounds are especially new, the structural elucidation must be accomplished *with extremely great care* even by using elemental analysis, high resolution mass, ^{1}H- and ^{13}C-NMR. Actually, a novel high yield γ-chromone synthesis had been reported but a critical mistake was revealed. The compound acquired was proved to be *isomeric coumarin(Id) by an independent synthesis*.[3]

Therefore our findings will be disclosed for the coumarin/chromone discrimination by using ^{17}O-NMR(-100∼+700ppm)[4] for the first time. As shown in the Figure of ^{17}O-NMR of typical examples such as coumarin(1b) and its structural isomer(2g) in dimethyl sulfoxide (DMSO), there could be completely distinguished *two* ^{17}O chemical shifts(phenolic ether or ester oxygens and carbonyl oxygens)[5] in (1b) from the others in (2g), which is thus entitled *the double-check technique*, while the single-check ^{13}C-NMR judgement is quite ambiguous owing to their very close carbonyl carbon chemical shifts(173.6ppm in (1b) and 176.8ppm in (2g)).[6] Yet more important, in addition, the δ(C=O)-δ(-O-) values (Δppm) were found easier by far to be differentiated from each other, *i.e.*, 126-136ppm for coumarin(1b) and 275-282ppm for chromone(2g), *almost never depending on the solvents or temperature*, from the data



Coumarin(1) Chromone(2)

	R^1	R^2	R^3	R^4	R^5	R^6
a	H	CH_3	CH_3	Br	CH_3	H
b	H	CH_3	CH=CH-CH=CH		H	H
c	COOH	H	H	H	H	H
d	CONH $CO_2CH_2CH_3$	H	H	H	H	OCH_2CH_3
e	NO_2	CL	H	H	H	H
f	CH_3	H	CH_3	Br	CH_3	H
g	CH_3	H	CH=CH-CH=CH		H	H
h	H	CHO	H	H	H	H
i	H	CN	H	H	H	H

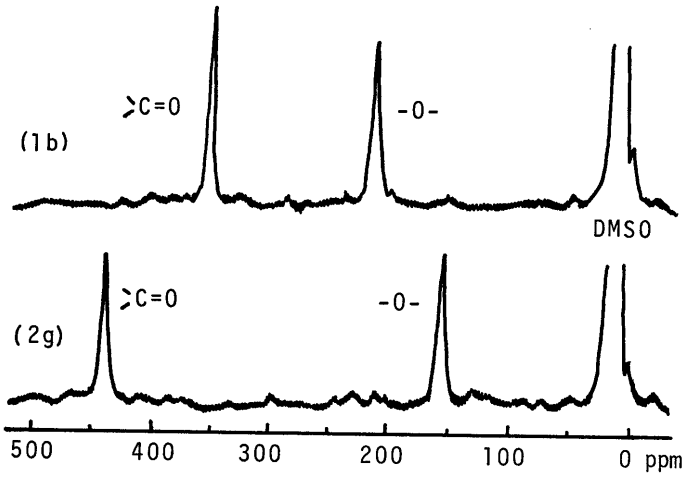


Fig.1. ^{17}O-NMR spectra of Coumarin(1b) and Chromone(2g) on 1.5 M solution in Dimethyl sulfoxide(DMSO) at 100°C

Table I. Temperature and Solvent Effects on the ^{17}O Chemical Shifts(δ) of Coumarin(1b) and Chromone(2g)[a]

	Compound					
	1b			2g		
	δ(C=O)	δ(-O-)	Δ[b]	δ(C=O)	δ(-O-)	Δ[b]
30°C						
$(CH_3)_2SO$	350.5	220.1	130.4	437.5	162.5	275.0
CH_3CN	345.7	219.4	126.3	437.1	160.7	276.4
$BrCH_2CH_2Br$	350.0	220.2	129.8	438.0	159.8	278.2
100°C						
$(CH_3)_2SO$	352.8	216.6	136.2	439.9	160.0	279.9
CH_3CN	351.9	216.3	135.6	439.7	159.4	280.3
$BrCH_2CH_2Br$	352.6	217.9	134.7	440.0	157.8	282.2

a) In ppm relative to internal dimethyl sulfoxide(DMSO: δ=13.0) on 0.5-2.0 M solution in each solvent.
b) Chemical shift differences, δ(C=O)-δ(-O-).

collected in Table I. As another nice and special instance, coumarin(1d)[3] gave six ^{17}O signals, from the complexity of which a pair of the corresponding *two* ^{17}O signals could be cleanly detected by applying these values, leading to be *coumarin* beyond all doubt. For generality of the judgement, ^{17}O-NMR spectra of other coumarins and chromones were recorded as indicated in Table II and a similar tendency can be verified.

In conclusion, it has been established, as shown in Table II, coumarin/chromone can be perfectly differentiated from each other by an unambiguous assignment of both the two ^{17}O chemical shifts and the δ(C=O)-δ(-O-) values between two signals regardless of whether the method and/or the compounds are new or not.

Table II. ^{17}O Chemical Shifts(δ)[a] of Coumarins(1a-e) and Chromones(2c-i) in Dry DMSO at 100°C

	Compound									
	(1a)	(1b)	(1c)[b]	(1d)[b]	(1e)[b]	(2c)[b]	(2f)	(2g)	(2h)[b]	(2i)
δ(C=O)	339.7	352.8	343.4	335.8	329.9	461.1	440.2	439.9	433.2	442.4
	(210)	(298)	(310)	(1116)	(435)	(396)	(285)	(350)	(513)	(813)
δ(-O-)	213.7	216.6	216.8	203.8	205.3	160.2	165.4	160.0	156.2	167.6
	(230)	(404)	(389)	(1080)	(477)	(350)	(250)	(234)	(300)	(548)
Δ[c]	126.0	136.2	126.6	132.0	124.6	300.9	274.8	279.9	277.0	274.9

a) In ppm relative to internal dimethyl sulfoxide(DMSO: δ=13.0) on 0.5-2.0 M solution. Values in parentheses indicate half-band widths($W_{1/2}$ in Hz).
b) Other oxygen-17 signals(δ): 259.4(COOH) in (1c); 63.9(OCH_2CH_3), 131.9 and 388.2($COOCH_2CH_3$), 273.8(CONH) in (1d); 615.5(NO_2) in (1e); 254.0(COOH) in (2c); 557.9(CHO) in (2h).
c) Chemical shift differences, δ(C=O)-δ(-O-).

ACKNOWLEDGEMENT Partial financial support from the Fujisawa Foundation(to K.N.) is gratefully acknowledged.

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5) a) All the spectra were measured at natural abundance on a JEOL GX-270 or GX-400 spectrometer operated at 36.6 or 54.2 MHz with a chemical shift range from δ=-100 to +700, 8K data points after zero-filling, 45° pulse angle, and 20 or 40 ms acquisition time. The number of scans was from 2×10^4 to 1×10^6 depending on the concentration and line widths of the sample. After recorded, all of the samples were recovered pure in more than 90% yield by dilution with water or by evaporation *in vacuo* followed by recrystallization. Dry dimethyl sulfoxide(DMSO) at 100°C, as in the text, is the solvent of choice, leading to the best resolved spectra owing to high concentration of the samples; b) All the compounds in this letter were prepared by the literature methods[1-3] or are from commercial sources. The parent coumarin and chromone gave each one pair of ^{17}O signals at 347.7/ 216.2 and 442.5/155.8 ppm, respectively and other ^{17}O signals such as phenolic and alcoholic hydroxyl and their alkyl ethers, as commonly seen in the natural flavonoids, appear in 20-110ppm, which does not disturb the judgement in the text. A full detail will be reported elsewhere.

6) Generally, the carbonyl carbon signals in ^{13}C-NMR appear in 155-165ppm for coumarins and in 175-185ppm for chromones. However, the presence of the bulky substituents(R^2 and R^3), especially in coumarin or the presence of other carbonyl carbons like amide and ester and of oxygen-bearing quaternary carbon as in (1d) gave rise to serious confusion. For up-to-date references on ^{13}C-NMR, see the following. E. Breitmaier and W. Voelter, 'Carbon-13 NMR Spectroscopy,' 3rd, completely revised edition, VCH Verlagsgesellschaft, Weinheim, 1987; P.K. Agrawal(ed.),'Carbon-13 NMR of Flavonoids,' Elsevier Science Publishers B.V., Amsterdam, 1989.

(Received October 21, 1992)